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RECENT INVESTIGATIONS ON THE PHYSIOLOGICAL BASIS OF EMOTIONS*

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A discussion of the problem of emotion takes naturally as its origin the ideas which Walter B. Cannon developed a number of years ago, and I would like to start with the discussion of a diagram (1) which summarizes Cannon's ideas on these matters. In the diagram it is shown that the thalamus is activated by afferent stimuli. These impulses are relayed to other parts of the diencephalon and result in a "downward discharge" activating viscera and skeletal muscle. In addition, they elicit an "upward discharge" which is the equivalent of the "feeling tone" of the emotion. Cannon assumed further that there would be an "upward discharge" to the cortex of the brain which would diminish the inhibitory action of this structure on the thalamus or on the hypothalamus. This is the general scheme and I will follow it and try to implement it by the work which has been done in the intervening years.

Cannon's finding that the "downward discharge" involves the sympathetico-adrenal system is common knowledge today and will not be further pursued (2). However, it should be mentioned that the visceral discharge which occurs in emotion is not restricted to the sympathetico-adrenal system but concerns the vago-insulin system as well. This was shown in two groups of experiments (3). In the first, normal, adrenodemedullated and adrenodemedullated-vagotomized rats were exposed to noise and the blood sugars were determined. As was to be expected the normal rats showed an increase in blood sugar but the adrenodemedullated animals a decrease. The latter phenomenon suggested an activation of the internal secretion of the pancreas via the vagus. Consequently

* Aided in part by the Office of Naval Research.

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adrenodemedullated rats in which the vagi had been sectioned below the diaphragm were tested and were found to show no changes in blood sugar under conditions of emotional excitement. If rats were tied to an animal board the emotional excitement resulting from struggle gave likewise evidence for a sympathetico-adrenal and vago-insulin discharge.

Experiments on cats in which the effect of the sympathetico-adrenal discharge on the blood sugar was prevented by transection of the spinal cord at the cervical level showed, under conditions of emotional excitement and on stimulation of the hypothalamus, a fall in blood sugar which was eliminated by vagotomy. These experiments likewise indicate that, as the result of proper environmental stimuli, or because of direct electrical stimulation of the hypothalamus, emotional excitement induces a vago-insulin and sympathetico-adrenal discharge. Since in the normal animal the blood sugar rises under these conditions it may be said that the sympathetico-adrenal system predominates over the vago-insulin discharge if the changes in blood sugar are taken as an indicator of the central autonomic balance.

The action of emotion on the human organism exemplified by studies on normal and psychotic individuals should now be mentioned. It was known from earlier work (4; 5) that excited psychotics have a normal blood sugar while normal individuals show hyperglycemia in emotional excitement. This suggests that the reactivity of the autonomic centers is altered in psychotics. In order to gain further insight into these relations a method was developed which allowed the assay of minute amounts of insulin in the blood. The hypophysectomized-adrenodemedullated rat was found to be a suitable test animal for this purpose (6). In addition, such a rat reacts to the injection of adrenalin like an unoperated animal with a hyperglycemia. If blood containing both insulin and adrenalin is injected and the effect on the blood sugar of the test animal is determined, the relative balance between insulin and adrenalin in that blood can be ascertained. In such studies it was found that the blood obtained from the excited mental patients (7) produces a hypoglycemic reaction in the test animal accompanied by typical hypoglycemic symptoms such as lack of righting reflexes and occasionally hypoglycemic convulsions. The analyses of the

blood sugars of the test animals showed very low values (29–40 mg percent). In no case was a value observed similar to those obtained when the blood of nonexcited normal persons or psychotic patients was injected into the test animal. It is concluded from these observations that in the blood of the excited psychotic patients the insulin/adrenalin ratio is greater than normal. Since in emotional excitement the blood of the patients does not show any increased blood sugar, it is inferred that the shift in the insulin/adrenalin ratio is largely due to a diminished reactivity of the sympathetico-adrenal system with consequent lessened adrenalin content of the blood in emotion. On the other hand, normal individuals subjected to mild excitement do not show any measurable amounts of insulin in the blood and their blood sugar rises.

Two conclusions may be drawn from these experiments:

1. Emotion is accompanied by a discharge of the vago-insulin and sympathetico-adrenalin systems.
2. The sympathetico-adrenalin system predominates over the vago-insulin system in physiological conditions but a marked quantitative alteration occurs in psychotics leading to a relative predominance of the vago-insulin system in emotion.

These findings suggest the problem to determine what physiological factors modify the reactivity of the autonomic centers and thereby the balance which physiologically exists between the centers activating the vago-insulin and the sympathetico-adrenalin systems respectively. By using the previously described methods on rats it was found that the reactivity of sympathetic autonomic centers decreases with increasing age (8). Furthermore it was shown that administration of thyroxin increases their reactivity and that thyroidectomy is accompanied by a lesser responsiveness of these centers (9).

It was mentioned earlier that Cannon has thoroughly established the sympathetico-adrenalin discharge as one of the characteristics of the "downward discharge" occurring with emotion. There is evidence that the secretion of adrenalin in turn initiates still further changes. The injection as well as the secretion of adrenalin affects the rate of secretion of the adrenal cortex as can be shown by using the number of circulating lymphocytes as an indicator.

Injection of as little as 0.05 gamma of adrenalin for each 100 grams of rat induces a marked lymphopenia (10). This enormous sensitivity of the lymphopenic reaction to adrenalin made it probable that the secretion of adrenalin may also have a similar effect. Numerous experiments showed that the secretion of adrenalin is followed by lymphopenia (11). For the topic of this paper it is particularly relevant to report that emotional excitement (rage) induced in rats by a slight shock—not a convulsive shock—is accompanied by lymphopenia. However, this reaction occurs only in normal rats, not in adrenodemedullated or adrenalectomized rats. For a further analysis of this phenomenon it should be mentioned that lymphopenia results from the injection of the adrenotropic hormone of the anterior pituitary into the normal but not into adrenalectomized rats (12). Moreover, adrenodemedullated animals show a lymphopenia on injection of minute quantities of adrenalin whereas no change in lymphocyte count is observed in adrenalectomized rats under these conditions. From these observations it seems to follow that emotional excitement leads to a sympathetico-adrenal discharge which in turn initiates an activation of the adrenal cortex via the anterior hypophysis.

These findings show clearly that the changes occurring in the endocrine system in emotion are more profound than was formerly assumed. But there is evidence for additional change in the secretory activity of the hypophysis. Emotional excitement leads also to an increased secretion of the antidiuretic hormone from the posterior lobe of the hypophysis (13). This effect persists in spite of the denervation of the kidneys and the adrenals and the removal of the abdominal sympathetic chains. The reduction of urinary flow seen in hydrated animals in excitement can be matched by the injection of posterior pituitary extracts, and these results have been shown to be valid in man (14).

This reaction is obviously independent of the secretion of adrenalin and seems to be caused by a hypothalamic-hypophyseal discharge. In agreement herewith, is the observation of O'Connor (15) that transection of the stalk abolishes the inhibition of water diuresis in emotional excitement. In addition we know that at least certain forms of emotional excitement lead to an excitation

of the anterior lobe of the hypophysis. A number of investigators (16, 17) showed that in the rabbit, under the conditions of sexual excitement, an increased secretion of the gonadotropic hormones of the anterior pituitary occurs which causes ovulation. This activation of the anterior hypophysis leads to a diminution in the amount of luteinizing hormone which can be assayed in this gland (18). These effects are absent after transection of the hypophyseal stalk.

I have presented this material in order to emphasize the fact that the "downward discharge" is far more than the sympathetico-adrenal change which Cannon described. It concerns both branches of the autonomic system, the parasympathetic as well as the sympathetic, and involves directly or indirectly the greater part of the endocrine system as well since the rate of secretion of the anterior and posterior part of the pituitary and of the adrenal cortex may be altered.

These findings are also of interest from another point of view. It was stated that in the rabbit sexual excitement alters the rate of secretion of the anterior pituitary hormones. Whether or not the rate of secretion of gonadotropic hormones is altered in other forms of emotion is not known. However, it seems not unlikely that the neuro-endocrine pattern of the "downward discharge" is different in various forms of emotional excitement.

Let us return to the relation existing between the parasympathetic and sympathetic system in emotion, but instead of studying emotion as a result of appropriate environmental stimuli let us consider briefly the effects of electrical stimulation of the hypothalamus resulting in sham rage (Ranson, Hess, and many others, cf. 2).

Although it is known that parasympathetic effects are preferably obtained from the anterior, and sympathetic effects from the posterior part of the diencephalon (Hess and others, 19), it is possible to obtain evidence for both parasympathetic and sympathetic effects from the mammillary body. Electrical stimulation may result in maximal contraction of the sympathetically innervated nictitating membrane and in a marked slowing of the heart rate (20). Since the latter effect disappears after vagotomy and since the former is due to sympathetic impulses only, this observation

shows simultaneous parasympathetic and sympathetic discharges as a result of the stimulation of a circumscribed area in the hypothalamus.

Sympathetic effects occurring in emotion have received the greatest attention as a result of the fundamental work of Cannon and his collaborators. However, parasympathetic effects in emotion, particularly on the gastrointestinal tract, are well known in clinical medicine (2). Moreover vasodilatation as well as vasoconstriction of the face and also of the extremities (21) as a result of emotional excitement are established facts. The different types of vasomotor changes in the face which accompany various forms of emotion suggest some specificity in the autonomic "downward discharge." Such an interpretation seems to be supported by the recent work of Wolf and Wolff (22) on gastric secretion in a patient with a gastric fistula which allowed the direct observation of vascular and secretory changes. The results of this work may be summarized as follows: motor activity, vascularity, and secretion of hydrochloric acid are increased not only under conditions of "pleasurable thoughts of eating" but also in situations calling forth "aggressive feelings including resentment, hostility and anxiety." At the same time a flushing of the face was observed and the mucous membrane of the nose showed increased secretion and hyperemia (23).

In contradistinction to these signs of parasympathetic excitation the authors observed in the same person that conditions of fear exert exactly the opposite effects on the gastric mucosa and the motility of the stomach. These studies suggest that fear causes predominantly sympathetic discharges, and feelings of hostility and anxiety cause largely parasympathetic discharges. In line with this interpretation is another interesting observation of Wolf and Wolff that anxiety fails to produce the described effects on the stomach after vagotomy.

Not only the autonomic but also the somatic part of the "downward discharge" may show some degree of specificity. The rage reaction of the cat, already described by Darwin and seen also under conditions of hypothalamic stimulation, is accompanied by a motor discharge which seems to prepare the animals for fight (unsheathing of the claws, etc.), but it is also known that under conditions of extreme fear an entirely different reaction may be

observed. In terror a person may feel unable to move although sympathetic excitation may persist as in rage. It is interesting to relate these psycho-physiological experiences to the experiments of W. K. Smith (24) who on stimulation of the limbic area 24 located on the medial side of the brain obtained sympathetic discharges such as pupillary dilatation, rise in blood pressure and piloerection, and at the same time noted a complete relaxation of all extremities.* At that time I suggested to Dr. Smith that the reaction he had been studying may underlie the emotional experience of extreme fear and terror. This interpretation appears to be confirmed by recent work of Ward (25) who removed area 24 bilaterally in cats with the result that these animals no longer showed any fear reactions.

It would be interesting to know whether the rage reactions are unchanged in such animals. Although the answer to this question is not known, the observations suggest that the somatic "downward discharge" shows specific differences in different types of emotional excitement. This is in agreement with common experiences and the clinical work of Duchenne (26) who showed by stimulation of the muscles of the face that facial expression accompanying different moods and feelings is the result of excitation of different muscles or groups of muscles.

The next phase of the problem which Cannon envisaged is the "upward discharge" from the hypothalamus to the cortex. It may be demonstrated by several methods. In cats anesthetized with dial-urethane, potentials recorded from various cortical areas appear largely in the form of grouped potentials similar to those seen in sleep. If a certain part of the cortex is excited, these grouped potentials disappear and are replaced by potentials of smaller amplitude and higher frequency, and on cessation of stimulation the grouped dial potentials reappear. Whereas excitation of a specific sense organ produces signs of excitation confined to its specific cortical projection area, stimulation of the hypothalamus induces excitation in all cortical areas. The effects are bilateral but the action on the ipsilateral side is stronger (27). Similar

* The latter reaction appears to be due to activation of a cortical suppressor area.

results are obtained when the effect of hypothalamic stimulation on the cortex is studied after various cortical areas had been strychninized by topical application of minute pledgets soaked in strychnine solution. The increase in the number of strychnine spikes and the disappearance of grouped spikes on hypothalamic stimulation indicate again cortical excitation in all cortical areas.

Some insight into the anatomical structures involved in the transmission of impulses from the hypothalamus to the cortex is gained by means of the strychnine method (neuronography) which Dusser de Barenne and McCulloch applied so successfully to the exploration of cortico-cortical interconnections (28). In Murphy and Gellhorn's (30) experiments strychnine was injected into the hypothalamus and the appearance of spikes was recorded in subcortical and cortical structures. It was found that, first, the dorsomedial nucleus of the thalamus was fired and then the cortex on the same side. Later spikes appeared in the contralateral hypothalamus, the dorsomedial nucleus, and finally the cortex. The ventrolateral thalamic nucleus remained constantly negative under these conditions. From these experiments it is inferred that the transmission of impulses from the hypothalamus to the cortex involves principally the dorsomedial thalamic nucleus. Whether impulses can be transmitted from the hypothalamus to the cortex without interruption in the thalamus is as yet undecided (cf. also the anatomical studies of LeGros Clark, 31, and others, 32). These experiments seem to furnish us at least with the blueprint of the anatomic and physiologic basis of the "upward discharge" referred to at the beginning.

The inhibitory action of the cortex on subcortical structures remains to be discussed. Since the memorable work of Goltz (33) it has been known that removal of the cortex greatly increases emotional reactivity in experimental animals. These investigations were confirmed and extended by Cannon and Bard who showed that the center of autonomic and somatic reactions elicited under conditions of emotional excitement is located in the posterior part of the diencephalon and that this structure is normally inhibited by the cortex. Cannon assumed as mentioned earlier that this inhibitory action is diminished as a result of cortical excitation. In other words he believed that two types of "upward discharges" were

present, the first representing the physiological basis of the alteration in "feeling tone" of perceptions under conditions of emotion, the second diminishing the intensity of inhibition which normally is exerted by the cortex on subcortical structures and particularly on the hypothalamus. Our investigations have given no evidence for such division of the "upward discharges." However, it could be shown that the restricting power of the cortex concerns not only the hypothalamic "downward" but also the hypothalamic-cortical "upward discharge." This is illustrated by the following experiment.

If a minute amount of strychnine is injected into the hypothalamus small spikes may be recorded from this structure while various cortical areas show their normal activity.* There exists frequently a high degree of asynchrony between the activity of various cortical areas as well as between cortex and hypothalamus. However, if anoxia or asphyxia is induced, a synchronous spike discharge occurs in the hypothalamus and in all parts of the cortex *after* cortical activity had been greatly reduced or completely eliminated (34). This experiment, which may be repeated several times in the same animal with similar success, indicates that the hypothalamus may act as a pacemaker of the entire brain (including the cerebellum) only if cortical activity has been greatly reduced. The inhibitory power of the brain appears to be a function of cortical excitability; with decreasing activity of the cortex this influence on the diencephalon is diminished. The increased emotional reactivity in various forms of anoxia and in the precomatose stages of hypoglycemia may be interpreted on this basis.

Finally the question remains to be discussed how emotional excitation can be aroused. Cannon suggested that impulses from peripheral receptors are relayed in the thalamus and may cause excitation of the diencephalon. This is indeed the case as can be shown by the study of hypothalamic action potentials under the influence of nociceptive stimuli. Mechanical or electrical stimulation of the sciatic will cause distinct changes in hypothalamic action potentials which are indicative of excitation (29). It should

* For the sake of clarity we disregard the occasional occurrence of a spike transmitted to the cortex from the hypothalamus.

be added that excitation of the higher senses (eye, ear) may likewise arouse emotional excitation. The physiological basis of this phenomenon seems to lie in the fact that strychninization of cortical projection areas and association areas may cause firing of the hypothalamus (30). The appearance of strychnine spikes in the dorsomedial and the ventrolateral nuclei suggests that these parts of the thalamus furnish an intermediary station in the transmission of cortico-hypothalamic impulses. These data furnish the neurological background for the common assumption, founded on observations on man and animals, that emotional excitement, and the autonomic phenomena accompanying it, may be called forth by sensations of different modalities.

Summary

The process of emotion results in the activation of the hypothalamus which in turn discharges "upwards" and "downwards." The "downward discharge" involves not only the sympathetic system but the parasympathetic division of the autonomic system as well. The former activates the adrenal medulla as was established through the classic investigations of Cannon and his collaborators; the latter activates the islets of Langerhans. In emotion the secretion of insulin is increased via the vagus but its action on the blood sugar is obscured normally through the dominance of the sympathetico-adrenal discharge. However, experiments on mental patients under conditions of emotion suggest a relative predominance of the vago-insulin system in these cases. Further experiments show that the rate of secretion of hormones of the pituitary gland and of the adrenal cortex is likewise altered in emotion. Emotional excitation causes hypothalamic-posterior pituitary discharges leading to increased liberation of the antidiuretic hormone (Verney et al.), whereas certain forms of excitement related to sexual activity have been shown to link hypothalamic excitation with increased secretion of the gonadotropic hormones of the anterior pituitary (Westman and Jacobson). It was shown also that in animals subjected to emotional excitement there is an increased secretion of hormones of the adrenal cortex which is initiated by the secretion of adrenalin and results in lymphopenia.

These autonomic-endocrine discharges are accompanied by either

excitation or inhibition of striated muscles. The former is associated with rage, the latter, involving excitation of the cortical suppressor area 24, with fear or terror.

The long-postulated "upward discharge" from the hypothalamus to the cortex was established by several procedures. First, it was shown that stimulation of the mammillary body leads in the anesthetized cat to bilateral cortical excitation which is characterized by disappearance of dial potentials and appearance of faster potentials of lower amplitude (lessened synchrony of cortical discharge). Second, experiments with the strychnine method of Dusser de Barenne indicated that this hypothalamic-cortical discharge involves most commonly the dorso-medial nucleus of the thalamus as relay station. In addition the excitation spreads to the contralateral hypothalamus and from there via the thalamus to the cortex.

The conditions which determine this "upward discharge" were further elucidated by the observation that injection of strychnine into the hypothalamus leads to a generalized synchronous strychnine discharge in all parts of the cerebral cortex, when, as a result of asphyxia, the cortical potentials are greatly reduced in amplitude or have disappeared completely. These experiments prove that normal cortical activity holds in abeyance not only the "downward discharge" from the hypothalamus, as is known from observations on animals with sham rage, but the "upward discharge" to the cortex as well.

Excitation of the hypothalamus through nociceptive impulses accounts for emotion resulting from pain while the appearance of hypothalamic spikes after strychninization of a cortical area illustrates activation of the hypothalamus from the cortex. This is the basis of emotional excitement following various sensations and associations linked with them.

It is suggested that (*a*) the autonomic-endocrine and the somatic "downward discharge" and (*b*) the hypothalamic-cortical "upward discharge" represent the basic physiological pattern of the emotional process. The former is the basis of the bodily expression of emotion; the latter accounts for the "feeling tone" and for the mental changes which accompany emotion. The different types of facial expression (Duchenne), the fact that rage involves activation

and fear inhibition of the skeletal muscles, and the specific vascular and secretory changes (E. Weber, Wolf and Wolff) in different forms of emotion reflect the great variability in the pattern of the somato-autonomic discharge. It is probably paralleled by similar specific hypothalamic-cortical discharges which underlie the manifold forms of subjectively experienced emotion.

The quantitative determination of the neurological components (somatic, parasympathetic and sympathetic) and of the endocrine components of these specific patterns seems to be one of the chief tasks for a future physiology and pathology of emotion.

REFERENCES

1. BARD, P.: Emotion. In Handbook of General Experimental Psychology. Clark Univ. Press, 1934.
2. GELLHORN, E.: Autonomic Regulations. New York, Interscience, 1943.
3. GELLHORN, E., CORTELL, R. and FELDMAN, J.: Am. J. Physiol., *133:* 532, 1941.
4. WHITEHORN, J. C.: Am. J. Psychiat., *13:* 987, 1934.
5. GILDEA, E. F., MAILHOUSE, V. L. and MORRIS, D. P.: Am. J. Psychiat., *92:* 115, 1935.
6. GELLHORN, E., FELDMAN, J. and ALLEN, A.: Endocrinol., *29:* 137, 1941.
7. ——, —— and ——: Arch. Neurol. & Psychiat., *47:* 234, 1942.
8. —— and BALLIN, H. M.: Proc. Soc. Exp. Biol. Med. *68:* 540, 1948.
9. —— and FELDMAN, J.: Endocrinol., *29:* 467, 1941.
10. —— and FRANK, S.: Proc. Soc. Exper. Biol. & Med., *69:* 426, 1948.
11. —— and ——: Proc. Soc. Exper. Biol. & Med., *71:* 112, 1949.
12. DOUGHERTY, T. F. and WHITE, A.: Endocrinol., *35:* 1, 1944.
13. VERNEY, E. B., Proc. Roy. Soc., London, S. B., *135:* 25, 1947.
14. KELSALL, A. R.: J. Physiol., *109:* 150, 1949.
15. O'CONNOR, W. J.: Quart. J. Exp. Physiol., *33:* 149, 1946.
16. WESTMAN, A. and JACOBSOHN, D.: Acta obst. et. gynec. Scandinav., *17:* 235, 1937.
17. BROOKS, C. M.: Am. J. Physiol., *121:* 157, 1938.
18. —— and LAMBERT, E. F.: Am. J. Physiol., *128:* 57, 1939.
19. HESS, W. R.: Vegetative Funktionen und Zwischenhirn. Basel, Benno Schwabe, 1947.
20. GELLHORN, E., CORTELL, R. and MURPHY, J. P.: Am. J. Physiol., *146:* 376, 1946.
21. WEBER, E.: Der Einfluss psychischer Vorgänge auf den Körper. Berlin, J. Springer, 1910.
22. WOLF, S. and WOLFF, H. G.: Human Gastric Function. Oxford Univ. Press, 1947.

23. WOLFF, H. G., HOLMES, T. H., GOODELL, H. and WOLF, S.: Tr. A. Am. Physicians, *59:* 88, 1946.
24. SMITH, W. K.: J. Neurophysiol., *8:* 241, 1945.
25. WARD, A. A.: J. Neurophysiol., *11:* 13, 1948.
26. DUCHENNE, G. B.: Physiology of Motion. Philadelphia, Lippincott, 1949.
27. MURPHY, J. P. and GELLHORN, E.: J. Neurophysiol. *8:* 341, 1945.
28. MCCULLOCH, W. S.: In Precentral Motor Cortex. Ed. P. C. Bucy. Univ. of Illinois Press, 1944.
29. GELLHORN, E. and BALLIN, H.: Am. J. Physiol., *146:* 630, 1946.
30. MURPHY, J. P. and GELLHORN, E.: J. Neurophysiol., *8:* 431, 1945.
31. LEGROS CLARK, W. E.: Hypothalamus. Edinburgh, Oliver and Boyd, 1938.
32. INGRAM, W. R.: Research Publ., A. Nerv. & Ment. Dis., *20:* 195, 1940.
33. GOLTZ, F.: Arch. f.d. ges. Physiol., *51:* 570, 1892.
34. GELLHORN, E.: Proc. Soc. Exper. Biol. & Med., *70:* 107, 1949.